May 20, 2004

Cynthia Graham, Ph.D.
Technical Contact
Bayer CropScience LP
100 Bayer Road
Pittsburgh, PA 15205

Dear Dr. Graham:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for O,O-Diethyl Dithiophosphate posted on the ChemRTK HPV Challenge Program Web site on January 7, 2004. I commend Bayer CropScience LP for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Bayer CropScience LP advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
O,O-Diethyl dithiophosphate

Summary of EPA Comments

The sponsor, Bayer CropScience LP, submitted a test plan and robust summaries to EPA for O,O-Diethyl dithiophosphate (CAS No.298-06-6), dated November 26, 2003. EPA posted the submission on the ChemRTK HPV Challenge Website on January 7, 2004.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The submitter needs to provide measured melting point and vapor pressure data, and address a discrepancy concerning the water solubility data for this chemical.

2. Environmental Fate. The submitter needs to provide data on hydrolysis in water at environmental pH and ambient environmental temperatures for this chemical. The submitter also needs to provide measured ready biodegradation data for this chemical.

3. Health Effects. For the purposes of the HPV Challenge Program, the submitted data on acute toxicity appear adequate but the robust summaries need to be enhanced. The gene mutation data need to reflect more recent data that are publicly available in EPA's files. The submitter's proposal for reduced health endpoint testing based on a closed-system intermediate claim was not adequately supported. Therefore, data gaps exist for repeated-dose toxicity, genetic toxicity to the chromosome, and developmental/reproductive toxicity.

4. Ecological Effects. The submitted study for invertebrates is adequate for the purposes of the HPV Challenge Program. The submitter needs to perform acute toxicity testing for fish (the submitted study was on the sodium salt of the sponsored chemical), and algae in accordance with OECD test guidelines.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on O,O-diethyl Dithiophosphate Challenge Submission

General

The submitter included a separate, confidential business information (CBI) claim that the sponsored chemical was a closed-system intermediate. EPA reviewed this information and determined that the claim was not supported.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for boiling point, and octanol/water partition coefficient are adequate for the purposes of the HPV Challenge Program.

Melting Point. The submitter did not provide a melting point for this chemical, but states that it is a liquid at ambient temperature. This information is inadequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured melting point data for this chemical following OECD TG 102. The submitter may provide calculated data only if the melting point data is under 0 °C.

Vapor Pressure. The submitter provided a calculated vapor pressure of .077 hPa (0.058 mm Hg). This value is not adequate for the purposes of the HPV Challenge Program. Estimated values are only acceptable in cases where the value is less than 1 x 10^{-5} Pa (less than 1 x 10^{-8} mm Hg) at 25 °C. The submitter needs to provide measured vapor pressure data for this chemical following OECD TG 104.

Water Solubility. The submitter indicates in its robust summary that this chemical is not soluble in water. Qualitative descriptions (e.g., very soluble, insoluble) are not adequate for the purposes of the HPV Challenge Program. Furthermore, EPA was able to find a solubility value of 64,000 mg/L in water (Chemical Inspection and Testing Institute, Biodegradation and Bioaccumulation Data of Existing Chemicals based on the CSCL Japan, Japan Chemical Industry Ecology - Toxicology and Information Center. ISBN 4-89074-101-1; 1992, 2-107). The submitter needs to address this discrepancy, or perform a water solubility test for this chemical following OECD TG 105.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The photodegradation and fugacity data provided by the submitter are adequate for the purposes of the HPV Challenge Program.

Stability in water. The submitter provided rate constants for the hydrolysis of this chemical in aqueous hydrochloric acid (concentrations ranging from 0.1 M to 7 M) at 98 °C. The data provided by the submitter are not adequate for the purposes of the HPV Challenge Program. The data are not consistent with OECD guidelines which state that this endpoint should be measured at pH 4,7, and 9 and at ambient temperatures, or up to 50^{o} C in the screening test. The submitter needs to provide measured stability in water data for this chemical following OECD TG 111.

Biodegradation. The submitter calculated the biodegradability of this chemical using the BIOWIN program, and also provided two biodegradation studies using O,O-dimethyl ammonium phosphorodithioate (DMDTP) and O,O-diethyl ammonium phosphorodithioate as a surrogate for O,O-diethyl dithiophosphate. The studies used an acclimated activated sludge inoculum. Neither BIOWIN estimates nor inherent biodegradation data using DMDTP are adequate for the purposes of the HPV Challenge Program. However, EPA located ready biodegradation data from a MITI test for diethyl phosphorodithioate (Chemical Inspection and Testing Institute, Biodegradation and Bioaccumulation Data of Existing Chemicals based on the CSCL Japan, Japan Chemical Industry Ecology - Toxicology and Information Center. ISBN 4-89074-101-1; 1992, 2-107). The submitter can obtain the cited study and provide a robust summary of the information, or provide measured ready biodegradation data following OECD TG 301.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Acute Toxicity and Toxicity to the Gene. For the purposes of the U.S. HPV Challenge Program, these endpoints appear to have been met. See below for more information that needs to be provided in the submitted robust summaries. In addition to the Ames test summary provided, the submitter is encouraged to obtain, review, and summarize an Ames assay performed in 1986 and submitted to the EPA by a different company (see FYI-OTS-0887-0465).

Repeated-Dose Toxicity, Toxicity to the Chromosome, Reproductive Toxicity, and Developmental Toxicity. The submitter proposes to conduct a chromosomal aberration study (OECD TG 473) and a developmental toxicity study (OECD TG 414) based on a separate, CBI claim, that the sponsored chemical is a closed-system intermediate. EPA has determined (analysis not shown here) that this claim is not supported and thus, for the purposes of the HPV Challenge Program, the following endpoints are data gaps: repeated-dose, reproductive, and developmental toxicity (may be met with the single test protocol OECD TG 422 per HPV Challenge Program guidance and, as proposed by the submitter, a chromosomal aberration study following the OECD TG 473 protocol. In the event that the submitter can provide additional

information to fully support the closed-system intermediate claim, EPA would recommend that for the developmental toxicity test OECD TG 421 be used per HPV Challenge Program guidance instead of the proposed OECD TG 414.

Ecological Effects (fish, invertebrates, and algae)

The submitter needs to perform acute toxicity testing with the sponsored chemical (not the sodium salt of the acid) for fish and algae in accordance with OECD test guidelines. Although EPA agrees that the daphnid data show an aquatic toxicity concern, it is important to determine the sensitivity of vertebrates such as fish and aquatic plants such as algae to the sponsored chemical.

Specific Comments on the Robust Summaries

General

Most of the submitted robust summaries are of poor quality. The submitter should review the robust summary guidance document on the U.S. HPV Challenge website (http://www.epa.gov/chemrtk/robsumgd.htm **)**

Health Effects

Acute Toxicity. If available, the following information needs to be provided for acute toxicity robust summaries: number of animals, number of doses, number of deaths by dose, clinical signs and symptoms, necropsy results (all for the oral and inhalation summaries), and post-dosing observation period and year the study was performed (for oral, inhalation, and dermal studies).

Toxicity to the Gene. If available, the following information needs to be provided for the Ames test robust summary: doses used, presence/absence of cytotoxicity (and, if observed, at what dose), positive and negative controls used and their response in the study, the metabolic activation system used (inducer and species), and year the study was performed.

Ecological Effects

Fish. If available, the submitter needs to provide the following: concentrations used and whether they represent nominal or measured values, and the year the study was performed.

Invertebrates. If available, the submitter needs to provide the following: concentrations used and whether they represent nominal or measured values, test type (static or flow-through), number of organisms per dose, water quality parameters (dissolved oxygen, pH, hardness), and the year the study was performed.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.